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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,903	01/11/2002	David Michael Goldstein	R0038G-DIV	4961
24372	7590	03/15/2004	EXAMINER	
ROCHE PALO ALTO LLC				STOCKTON, LAURA
PATENT LAW DEPT. M/S A2-250				
3431 HILLVIEW AVENUE				
PALO ALTO, CA 94304				
				ART UNIT PAPER NUMBER
				1626

DATE MAILED: 03/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/045,903	GOLDSTEIN ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Laura L. Stockton, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 22 December 2003.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 2-16,22-31,33,38-40 and 42-45 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 2-7, 12, 16, 22-31, 33, 38-40 and 42-45 is/are rejected.
- 7) Claim(s) 8-11 and 13-15 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____ .
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ .	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
	6) <input type="checkbox"/> Other: _____ .

## **DETAILED ACTION**

**Claims 2-16, 22-31, 33, 38-40 and 42-45 are pending in the application.**

Rejections made in the previous Office Action which do not appear below have been overcome. Therefore, arguments pertaining to these rejections will not be addressed.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16, 22-31 and 42-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 16, under the definitions of R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup>, the “and” before the last substituent listed in each of the variable definitions should be changed to “or”.

Claims 43 and 44 do not conform to M.P.E.P. 608.01(m) since each claim must end with a period.

Claims 44 and 45 lack antecedent basis from claim 28. Claims 44 and 45 each claim “The compound of claim 28”, however, claim 28 is a method claim.

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection

based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2-6, 16, 22-24, 33 and 38-40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19-21 of U.S. Patent No. 6,376,527. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims in the patent differ only by generic description of the pyrazole product used in the method.

See, for example, the patent's claim 19 wherein R<sup>1</sup> is hydrogen, R<sup>2</sup> is hydrogen, A and B are each aryl, R<sup>3</sup> is heteroalkoxy, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are each hydrogen. One skilled in the art would thus be motivated to prepare pyrazole products embraced by the patent to arrive at the pyrazole products found in the instant claims with the expectation that the obtained pyrazole products would be useful in treating inflammatory

disorders such as arthritis. Therefore, the instant claimed method of using the pyrazole products would have been suggested to one skilled in the art.

### *Response to Arguments*

Applicants indicated that a terminal disclaimer would be filed when all other outstanding issues have been resolved.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2-7, 12, 33 and 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Faraci et al. {WO 94/13643}.

*Determination of the scope and content of the prior art (MPEP §2141.01)*

Applicants claim a method of treating a disease in a mammal treatable by administration of a p38 MAP kinase inhibitor (such as inflammation disorders) by administering pyrazole products.

Faraci et al. teach pharmaceutically active pyrazole products, that are structurally similar to the instant pyrazole products, that are administered in the instant claimed method. See in Faraci et al. (pages 1 and 2), for example, wherein A is  $-C(=O)$ , R<sub>1</sub> is amino, R<sub>2</sub> is alkyl, R<sub>3</sub> is phenyl substituted with hydroxy-alkyl and R<sub>4</sub> is phenyl. Also see, for example, the products on page 31, lines 5 and 12; page 39, line 11; and page 44, lines 12-14. Faraci et al. teach the pyrazole products are useful in treating disorders such as inflammatory disorders and immune suppression (page 5, lines 1-12).

*Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)*

The difference between the teaching in the prior art and the invention instantly claimed is that of generic description of the pyrazole products being administered for the intended use.

*Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)*

The motivation to make the pyrazole products derives from the expectation that structurally similar compounds would possess similar activity (e.g., an anti-inflammatory).

One skilled in the art would thus be motivated to prepare pyrazole products embraced by Faraci et al. to arrive at the pyrazole products found in the instant claims with the expectation that the obtained pyrazole products would be useful in treating inflammatory disorders such as arthritis. The instant claimed method of using the pyrazole products would have been suggested to one skilled in the art and therefore, the instant claimed invention would have been obvious to one skilled in the art.

*Response to Arguments*

Applicants' arguments filed September 22, 2003 have been fully considered. Applicants argue that: (1) in order to rely on a reference, the reference must be either in the field of Applicants' endeavor or be reasonably pertinent to the particular problem; (2) Faraci et al. disclose corticotropin release factor (CRF) antagonists and that CRF antagonists have never been shown to be effective in the treatment of p38 MAP kinase inhibitor related diseases such as arthritis, osteoarthritis, rheumatism or respiratory conditions; (3) the instant claimed compounds, such as Examples 27-30, show unexpected activity; and (4) compounds designed by modification of CRF antagonists, such as those of Faraci et al., could not be expected to inhibit TNF- $\alpha$  production as is achieved by the compounds of Applicants' invention.

All of Applicants' arguments have been considered but have not been found persuasive. Applicants claim a method of treating diseases by administering a p38 inhibitor. In Applicants' specification on page 35, lines 3-8, diseases which can be treated using a p38 inhibitor are

disclosed. Inflammatory diseases, as taught by Faraci et al., as well as Alzheimer's disease are embraced by Applicants' claims.

The difference between the methods of Faraci et al. and the methods instantly claimed is that the instant method utilize products which are generically embraced by the products of Faraci et al. Faraci et al. prepare specie which differ only at one position from the products instantly claimed. Applicants are treating the same disease by administering structurally similar pyrazole compounds. As stated in a previous Office Action, a compound and its properties are inseparable. *In re Papesch*, 137 USPQ 43 (CCPA 1963). Regarding Applicants' argument of unexpected results, Applicants have not provided factual support in a side by side showing that the compounds used in the instant method of use show unexpected, beneficial and superior results over the compounds taught in Faraci et al. Therefore, absent such showing, the instant claimed invention would have been obvious to one skilled in the art.

Applicants state that since the subject matter of claims 8-11, 13-15 and 25-31 was objected to for depending on a rejected base claim in the

Office Action of May 21, 2002, claim 16 has been amended to limit the definition of R<sup>3</sup> that was previously indicated as allowable. In response, the definition of R<sup>3</sup> in currently amended claim 16 is of a broader scope than the R<sup>3</sup> definition in claims 8-11, 13-15 and 25-31. Claim 16 is not allowable. See the obviousness-type double patenting rejection and the rejection under 35 USC 112, second paragraph, above.

***Allowable Subject Matter***

Claims 8-11 and 13-15 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Conclusion***

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE**

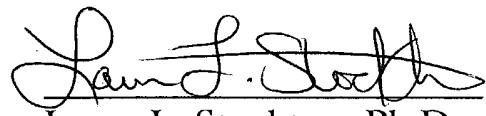
**FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:15 am to 2:45 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

The Official fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.



Laura L. Stockton, Ph.D.  
Patent Examiner  
Art Unit 1626, Group 1620  
Technology Center 1600

March 10, 2004